

Customer No. 31013

Atty Docket No. 056001-02943

## AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

1. (Original) A hepatocyte cell culture comprising liver cells in a bioreactor for use in a liver assist device comprising one or more hepatocytes having increased detoxification enzyme activity,

wherein the hepatocytes are isolated from a liver of a mammalian donor that had been administered at least one induction agent prior to isolation of the hepatocytes,

wherein the induction agent is selected from the group consisting of: beta-naphthoflavone, phenobarbital, 3-methylcholanthrene, ethanol, dexamethasone, arochlor 1254, 2,3,7,8-tetrachlorodibenzo-p-dioxin, phenothiazine, chlorpromazine, isosafole,  $\gamma$ -chlordane, allylisopropylacetamide, *trans*-stilbene oxide, kepone, acetone, isoniazid, pyridine, pyrazole, 4-methylpyrazole, pregnenolone 16 $\alpha$ -carbonitrile, troleandomycin, clotrimazole, clofibrate, clobuzarit, di(2-ethylhexyl)phthalate, and mono-(2-ethylhexyl)phthalate.

2. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is phenobarbital and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on BROW substrates which is about 20 to about 100-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

3. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is phenobarbital and wherein the thus induced hepatocytes have a functional cytochrome P450

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isozyme activity on PROD substrates which is about 2 to about 40-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

4. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is phenobarbital and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on 7-ethoxycoumarin substrates which is about 20 to about 50-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

5. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is phenobarbital and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on lidocaine which is about 10 to about 20-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

6. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is phenobarbital and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on lidocaine which is about 20 to about 50-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

7. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is beta-naphthoflavone and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on MROD substrates which is about 2 to about 10-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

8. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is beta-naphthoflavone and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on EROD substrates which is about 2 to about 10-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

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9. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is 3-methylcholanthrene and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on PROD substrates which is about 2 to about 10-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

10. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is 3-methylcholanthrene and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on MROD substrates which is about 2 to about 10-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

11. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is 3-methylcholanthrene and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on EROD substrates which is about 10 to about 20-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

12. (Original) The hepatocyte cell culture of claim 1, wherein the induction agent is 3-methylcholanthrene and wherein the thus induced hepatocytes have a functional cytochrome P450 isozyme activity on diazepam substrates which is about 2 to about 10-fold greater than hepatocytes isolated from a mammalian donor that was not administered an induction agent.

13. (Currently Amended) A bioreactor comprising:

a bioreactor chamber comprising a first region and a second region;  
a gas-permeable, liquid impermeable membrane defining said first region and said  
second region of said bioreactor chamber; and  
hepatocytes having increased detoxification enzyme activity,  
wherein the hepatocytes are isolated from a liver of a mammalian donor that had been administered at least one induction agent prior to isolation of hepatocytes,

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wherein the induction agent is selected from the group consisting of beta-naphthoflavone, phenobarbital, 3-methylcholanthrene, ethanol, dexamethasone, arochlor 1254, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, phenothiazine, chlorpromazine, isosafrole,  $\gamma$ -chlordan, allylisopropylacetamide, *trans*-stilbene oxide, kepone, acetone, isoniazid, pyridine, pyrazole, 4-methylpyrazole, pregnenolone 16 $\alpha$ -carbonitrile, troleandomycin, clotrimazole, clofibrate, clobuzarit, di(2-ethylhexyl)phthalate, and mono-(2-ethylhexyl)phthalate;

wherein the bioreactor can be used in a liver assist device.